REMARKS

Claims 7-14 and 19 are currently amended. Claim 17 is cancelled. Claim 21 is withdrawn. Upon entry of the present amendment, claims 1-16 and 18-21 are pending.

Support for the amendment of the claims is found throughout the specification and claims as originally filed. Amendment and cancellation of the claims here are not to be construed as an acquiescence to any of the rejections/objections made in the instant Office Action or in any previous Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the claims as originally filed, or substantially similar claims, in one or more subsequent patent applications.

Objection to the Specification

The objection to Figure 1 is overcome by the submission herewith of a replacement drawing that corrects the drawing to recite Figure 1A.

Objection to the Claims

The objection to claim 7 is overcome by the present amendment.

Although the Examiner acknowledges that Applicants have enabled fully complementary polynucleotides, the Examiner objects to claims 8-13 on the grounds that the term "antisense" raises enablement issues. Applicants respectfully disagree and traverse the rejection. Nevertheless, without acquiescing in any way to the rejection and in order to expedite prosecution of the application, the objection to claims 8-13 is overcome by the present amendment.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 14-20, which are directed to methods of screening compositions for opioid activity, are rejected under 35 U.S.C. § 112, first paragraph as lacking enablement on the grounds that the specification (i) fails to enable methods of compound screening where the control and test cell lines are different; and (ii) fails to enable methods of screening that involve the detection of neurohormones. Applicants respectfully disagree and traverse the rejection.

The first basis for the rejection is overcome by the present amendment, which makes clear that the cell-based compound screening methods involve screening compositions for opioid activity using cells that comprise a MOR-1 splice variant polypeptide relative to corresponding control cells that merely lack the MOR-1 splice variant polypeptide. Such assays are clearly enabled by the description in Applicants' disclosure. For example, Applicants' specification describes cell-based screening assays at page 43, under the heading "Characterization of Expressed Variants." In particular, Applicants describe cell-based assays for opioid binding, where CHO cells transiently transfected with mu opioid receptor splice variant polypeptides were contacted with an opioid, and binding of the opioid to the MOR-1 splice variant polypeptide was measured (page 43, limes 1-27). Opioid binding was compared between cells expressing variant polypeptides or corresponding control cells to determine whether the opioid bound with relatively high or low affinity (page 43, limes 1-27). Thus, this basis for enablement rejection should be withdrawn.

In the second basis for the enablement rejection, although the Examiner acknowledges that Applicants have enabled methods of screening using a [^{35}S]GTPγS binding assay to assess receptor signaling, the Examiner alleges that Applicants have failed to enable screening assays that detect neuroendocrine hormones. Applicants respectfully disagree.

Applicants' specification teaches that the opiate morphine interferes with the release of gonadotropin releasing hormone and corticotropin-releasing hormone from cells in the hypothalamus, thereby decreasing levels of luteinizing hormone, follicle stimulating hormone, adrenocorticotropin, and ß-endorphin (page 3, lines 15-25), but stimulates the release of pituitary hormones, such as prolactin (page 3, lines 15-25). In view of these effects on the neuroendocrine system, Applicants further teach that compositions may be screened for physiological effects on neuroendocrine levels (page 24, lines 25-29, and claims). This description is sufficient to enable Applicants' claimed screening methods.

The standard for enablement set forth in 35 U.S.C. 112, first paragraph, requires that Applicants provide a description of the invention sufficient "to enable any person skilled in the art to which it pertains . . .to make and use" the invention. The proper test of enablement is set forth in *United States v. Telectronics, Inc.*, (857 F.2d 778, 785, 8 USPQ2d at 1217, 1223 (Fed. Cir. 1988)):

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation.

Applicants' specification should not be read in isolation; rather, Applicants' specification must be read in light of the knowledge present in the art at the time of filing. "A patent need not teach, and preferably omits, what is well known in the art." M.P.E.P. 2164.01 Thus, compliance with the enablement standard does not require that Applicants describe methods known to the skilled artisan.

Methods of measuring hormone levels (*e.g.*, prolactin, growth hormone, gonadotropin-releasing hormone, adrenocorticotropin, corticotropin-releasing factor, luteinizing hormone, follicle stimulating hormone, testosterone or cortisol) were clearly well-known in the art at the time of filing as evidenced in the following Exhibits, which provide a description of such methods. For example, *Endocrinology: An Integrated Approach*, Nussey, S.S. and Whitehead, S.A. London: Taylor & Francis ; c2001; http://www.ncbi.nlm.nih.gov/sites/entrez?db=books&doptcmdl=TOCView&term=hormone+assay+AND+endocrin%5Bbook%5D (Exhibit A) describes methods for measuring luteinizing hormone and follicle stimulating hormone using ELISAs, radioimmunoassays, receptor binding assays, and bioassays. Methods for measuring prolactin, growth hormone, gonadotropin-releasing hormone, adrenocorticotropin, and corticotropin-releasing factor are also well known as shown in Exhibit B (GeneReviews, Pagon, Roberta A., Editor-in-chief; Bird, Thomas C.; Dolan, Cynthia R.; Smith, Richard J.H.; Stephens, Karen; Associate editors. Seattle (WA): University of Washington ; c1993, entitled *PROP1- Related Combined Pituitary Hormone Deficiency (CPHD)*), which clearly indicates that methods for detecting such hormones are in widespread clinical use. Similarly, Chen, *et al.* (*J Soc Gynecol Investig.* Abstract, 2004 Sep;11(6):393-8; Exhibit C) indicates that gonadotropin-releasing hormone can be readily measured using radioimmunoassays. Commercially kits are also available to measure levels of corticotropin-releasing factor, testosterone, and cortisol (Exhibit D, E, and F).

Given that methods for measuring neurohormones were well known in the art at the time of filing, Applicants have clearly enabled the claimed screening methods. Thus, this basis for the enablement should also be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 7, 19, and 20 for indefiniteness. Applicants respectfully disagree and traverse the rejection. However, without in any way acquiescing to the rejections/objections and in order to expedite prosecution of the application, the claims have been amended as set forth above, thereby obviating the rejection.

Specifically, claim 7 has been amended to recite that the polypeptide of SEQ ID NOs: 51, 53, 55, 57, 59, or 61 is a heterodimer or homodimer. Claim 19, from which claim 20 depends, has been re-written to more clearly and distinctly claim the invention. Claim 19 now recites a method of screening compositions for opioid binding activity that involves contacting a composition with an MOR-1 splice variant polypeptide of SEQ ID NOs: 51, 53, 55, 57, 59, or 61, contacting the MOR-1 splice variant polypeptide with an opioid, measuring binding of the composition and the opioid to the MOR-1 splice variant polypeptide; and comparing MOR-1 splice variant polypeptide binding of the composition to MOR-1 splice variant polypeptide binding to the opioid, where determination of binding of the composition is expressed relative to that of the opioid. Support for the amendment is found at Example 2, where Applicants describe the characterization of splice variants of the Oprm gene by analyzing the affinity of binding to various opioids (pages 46 and 47; and at claim 19 as originally filed). Accordingly, the indefiniteness rejection of claim 7, 19 and 20 should be withdrawn.

Allowable Subject Matter

Applicants acknowledge with appreciation that the Examiner has found that claims 1-6 satisfy the requirements for patentability.

CONCLUSIONS

In view of the above amendment, Applicants believe the application is in condition for allowance and respectfully request rejoinder of claim 21 and issuance of a Notice of Allowance of the application with claims. Should any issues remain or should the Examiner believe that a telephone conference with Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to contact the undersigned at the telephone number shown below.

Applicants believe that no fee is due to consider the present amendment. Nevertheless, the Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105.

Dated: October 27, 2008

Respectfully submitted,

By _____

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